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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,344	06/09/2005	Guy Vergnault	28069-608N01US	3745

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EXAMINER	
YOUNG, SHAWQUIA	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
10/14/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,344	VERGNAULT ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,18 and 21-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 18 and 21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-12, 18 and 21-27 are currently pending in the instant application. Applicants have amended claims 1, 4, 21, and 22 and cancelled claims 15-17 and 19 in an amendment filed on September 13, 2010. The finality of the previous Office Action has been withdrawn because of new prior art that has been found. Claims 1-12, 18 and 21-27 are rejected in this Office Action.

I. *Response to Arguments/Remarks*

Applicant's arguments, filed on September 13, 2010, have overcome the rejection of claims 1-5, 8,15-19 and 21-27 under 35 USC 103 as being unpatentable over Stefano (US 5,506,222) in view of Mueller, et al. in further view of DrugBank (http://redpollpharmacy.ualberta.ca/drugbank) and of Mehnert, et al. and zur Mtihlen, et al.; the rejection of claims 3-5 under 35 USC 103 as being unpatentable over Stefano in view of Muller, et al.; the rejection of claims 6-7 and 9-12 under 35 USC 103 as being unpatentable over Stefano in view of Muller, et al. in further view of Hansen (US 6,228,383) and Klein, et al. (US 6,013,637) and the objection of claim 19 as being of improper dependent form for failing to further limit the subject matter of a previous claim. The above rejections and objection have been withdrawn.

II. *Rejection(s)*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12,18 and 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vergnault (WO 02/102391) in view of Ekman,et al. (WO 87/02582) and Stefano (US 5,506,222) in further view DrugBank (http://redpoll.pharmacy.ualberta.ca/drugbank).

Regarding claims 1 and 2, the instant Application is drawn to a formulation comprising nanoparticles of spironolactone incorporated into a crystalline network of polar lipids wherein the nanoparticles of spironolactone have a mean diameter measured by photon correlation spectroscopy in the range of from about 300 nm to about 900 nm.

Vergnault teaches nanoparticles of spironolactone for use in a nanosuspension formulation wherein the nanoparticles have a mean diameter, measured by photon correlation spectroscopy, in the range of from about 300nm to about 900 nm, preferably 400 nm to 600 nm (see page 3, lines 20-24), but is silent regarding the crystalline network of polar lipids. Ekman, et al. teaches micro-capsule where an encapsulated hydrophobic or lipophilic substance is surrounded by polar solid crystals of polar lipids

which expose their hydrophilic face outwards and their hydrophobic face turned inwards towards the hydrophobic or lipophilic substance for topical application (See page 13, lines 30-36 and page 14, lines 1-5). Because spironolactone (7a-acetylthio-3- oxo-17a-pregn-4-ene-21,17-carbolactone) is practically insoluble in water and has a Log P of 4.3 (See Drugbank entry for Spironolactone), the lipid nanoparticulate form of the drug forms such that the lipid crystal shell's hydrophilic "side" would face "outward," because the hydrophobic "side" would face "inward" toward the encapsulated lipophillic nanoparticulate spironolactone. Stefano teaches a formulation comprising spironolactone for topical application (See column 1, lines 13-45).

The Ekman, et al. reference also teaches that when the micro-capsules in an ointment base is spread on mucous membranes (i.e., skin areas), the encapsulated substance will come into contact with lipophilic receptor surfaces in such a way that the crystals will slide away and open a contact path for the encapsulated oil phase or an lipophilic particle (See page 14, lines 1-5) which results in the direct contact of the lipophilic particle to the skin. It would have been obvious for one of ordinary skill in the art to combine the references Vergnault, et al. , Ekman, et al. and Stefano to prepare a micro-capsule formulation wherein nanoparticles of spironolactone are encapsulated in the capsules and used for topical application because of the advantages of using the micro-capsule taught by Ekman, et al. which allows direct contact of any lipophilic particle to the skin and its ability to alter solubility and surface properties (see page 4).

Regarding claims 8, 18, 23 and 24, Vergnault, et al, Ekman, et al and Stefano are discussed above, with Stefano teaching the use of topical spironolactone

compositions to treat the effects of increased androgenic activity including acne and hirsutism (abstract).Ekman, et al. teaches formulations that comprise micro-capsule which are crystalline and the lipid crystals which make up the micro-capsule are selected from a monoglyceride of a fatty acid having 12-18 carbon atoms or monglycerol ether. Vergnault, et al. teaches nanosuspensions comprising nanoparticles of spironolactone and the use of these nanosuspensions as a medicament adminstered by topical administration (See page 8, lines 10-14). Thus, it would have been obvious to the artisan of ordinary skill to combine the above references to prepare a micro-capsule formulation wherein nanoparticles of spironolactone are encapsulated in the capsules and used for topical application for treating skin conditions such as acne and hirsutism.

Regarding claim 3-5, the prior art of Ekman, et al teaches the lipid having a crystallization temperature of between ambient temperature (about 20ºC) and 100ºC (See page 5, lines 25-26). Ekman, et al. also teaches that the crystal lipids are from monoglyceride of a fatty acid having 12-18 carbon atoms or monglycerol ether having ether chains of the corresponding chain length or fatty acid esters of ascorbic acid (See page 5, lines 29-36) and that the monoglyceride can be selected from 1-monlaurin, 1-monomyristin, 1-monopalmitin and 1-monostearin or a mixture of two or more of these (page 6, lines 4-11).

Regarding claims 6 and 7, Ekman, et al. teaches that the crystalline polar lipids can be formed within a polar liquid such as glycerol, propylene glycol and ethylene glycol (See page 8, lines 9-37).

Regarding claims 9-12, Vergnault, et al. teaches a nanosuspension comprising nanoparticulate sipronolactone further comprise a stabilizer (see page 6, lines 14-24) wherein a preferred stabilizer is sodium docusate (see page 7, line 25).

Regarding claim 21, Ekman, et al teaches the process for preparing the micro-capsules comprising mixing the polar lipid with water or said polar liquid to the formation of a mixture, imparting to said mixture a temperature above the so-called transition temperature of the lipid and adding the hydrophobic or lipophilic substance being added before the lipid is transformed into liposome or while it is still in the liposomic form (See page 9, lines 8-29).

III. *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626